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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty's Docket No.: 101195-18

EXAMINER : A. Chakrabarti

GROUP ART UNIT: 1655

APPLICANT : Timo Hillebrand

APPLN. NUMBER : 09/454,740

FILED : December 6, 1999

FOR : Formulations and Method for Isolating Nucleic Acids from Optional Complex Starting Materials and Subsequent Complex Gene Analysis

Hon. Assistant Commissioner of Patents
Washington, D.C. 20231

AMENDMENT

Sir:

Please amend the above-referenced application as follows:

In the claims:

1. (amended) [Formulations without] A kit for isolating nucleic acids from complex starting materials in the absence of

chaotropic components by binding nucleic acid [with binding] to a substrate [solid phase, in particular of DNA, from optional complex starting materials containing], the kit comprising

[-a lysis/binding buffer system which contains at least one antichaotropic salt component,]

[-a solid phase,]

[-wash and elution buffers known as such]

a lysis/buffer system comprising at least one antichaotropic salt component, a substrate means for binding DNA, a wash buffer comprising at least 50% ethanol, and a low salt elution buffer.

2. (amended) The kit [formulations] according to claim 1, wherein the antichaotropic component is a salt chosen from the group consisting of [an] ammonium, [caesium] cesium, sodium and [/or] potassium [salt].

3. (amended) The kit [formulations] according to claim 1, wherein the lysis/binding buffer system contains detergents and additives.

4. (amended) The kit [formulations] according to claim 3, wherein the detergents and additives are chosen from the group consisting of tris-HCl, EDTA, polyvinyl pyrolidone, CTAB, triton

X-100, n-lauryl sarcosine, sodium citrate, DTT, SDS, and[/or] Tween.

B3

5. (amended) The kit [formulations] according to claim 1, wherein the lysis/binding buffer system contains an alcohol for binding to the substrate means [solid phase].

B4

6. (amended) The kit [formulations] according to claim 1, wherein the lysis/binding buffer system contains enzymes.

7. (amended) The kit [formulations] according to claim 1, wherein the lysis/binding buffer system is an aqueous solution.

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8. (amended) The kit [formulations] according to claim 1, wherein the lysis/binding buffer system is [a solid formulation] stable in storage in reaction vessels ready to use.

9. (amended) The kit [formulations] according to claim 1, wherein [all carriers serve as a solid phase which were used for isolation by means of] the substrate is chosen from the group consisting of chaotropic reagents, glass fiber mats, glass membranes, glasses, zeolites, ceramics, and silica carriers.

B6

10. (amended) The kit according to claim 1, wherein all carriers which have a negatively functionalised surface or functionalised surfaces which may be converted to a negative charge potential serve as the substrate means [solid phase].

B7

11. (amended) The kit [formulations] according to claim 10, wherein the surface of the carrier is modified by [an] at least one chosen from the group consisting of an acetyl group, carboxyl group [or] and hydroxyl group.

27. (amended) The kit [formulations] according to claim 1, wherein the lysis/binding buffer system contains [degrading proteins degrading enzymes] enzyme-degrading proteins.

B8

Please add the following new claim:

28. (new) The kit according to claim 1, wherein the complex starting material is chosen from the group consisting of compact plant materials, whole blood, tissue, microbioptate, paraffinne-coated materials, ercp-samples, swabs, foodstuffs, hair roots, cigarette butts, and food stains.

B9

29. (new) The kit according to claim 1, wherein the elution buffer comprises tris-HCl, TE, and water.

Please cancel claims 12-19. Applicant retains the right to file a divisional application to the non-elected invention of claims 12-19.

Remarks:

This is in response to an official office action dated July 20, 2000. Reconsideration in view of the following is respectfully submitted. A petition for a one month extension of the term is enclosed.

The applicant hereby affirms the election of Group I consisting of claims 1-11, 26, and 27.

The claims have been clarified to address the concerns of the examiner. The 'complex starting material' in claim 1 has been further defined in a dependent claim. The wash components and elution buffers have been clarified. Furthermore, claims 2, 4, 9, 11, and 27 have all been amended to conform to U.S. patent law practice.

The examiner objected to claims 1-5, 7 and 9 as being anticipated by the Anderson reference under 35 U.S.C. 102(e). Anderson discloses a cDNA that encodes for TIA-1 binding

proteins. The reference fails under anticipation analysis. Anderson does not teach a "means for binding DNA", as required in amended claim 1. Rather, the reference uses glass beads as an agent responsible for physically breaking down the yeast cells. The yeast cells are decomposed in a ball mill using the glass beads. The glass beads do *not* bind DNA as the glass membranes ("substitute means") do in the instant claims. Furthermore, according to Anderson, the precipitated DNA is not bound to the glass beads, but rather, the DNA is in the remaining supernatant and the glass beads are pelleted. The difference is illustrated in claim 1, where the claim requires a substrate means for binding the nucleic acid, an element that is absent from the Anderson reference. Since anticipation requires the reference to teach every element, the claims of the instant application are not anticipated.

The examiner further rejected claims 1-5 and 7-9 as being obvious under 35 U.S.C. 103(a) in view of the Anderson and Gonsalves references. Anderson was described above. Gonsalves discloses a protein or polypeptide of a grapevine leafroll virus. However, both Anderson and Gonsalves use proteinase K in conjunction with a centrifugation step in the isolation of DNA. Centrifugation is used to separate the components in the extract

based on their molecular weight. Thus, the proteinase and the nucleic acid can be separated based on these criteria.

A novel aspect of the instant application is that DNA is isolated in the absence of centrifugation, thereby saving a vast amount of time. It would be difficult to predict the potential effect of adding a proteinase, a proteolytic enzyme, to a mixture without the centrifugation step. The enzyme may mix with the nucleic acid extract and taint the experiment. However, the inventors of the instant application were able to negotiate this problem and still isolate the nucleic acid in the presence of the proteolytic enzyme without centrifugation. This result is a surprising one, not one that can be predicted by combining two references. Thus, the claims are not rendered obvious.

The examiner further rejected the claims under 35 U.S.C. 103(a) in view of Anderson and Summerton references. Anderson was described earlier. Summerton discloses compositions and methods for detecting and isolating nucleic acid sequences. Summerton is an inaccurate reference in this case. Summerton uses pH not as a technique to make a stable storage reaction vessel, but rather the reference uses pH to disrupt the DNA complex (col. 10, lines 38-9). Summerton states that the "addition of alkali to give a pH of 12 or above rapidly disrupts

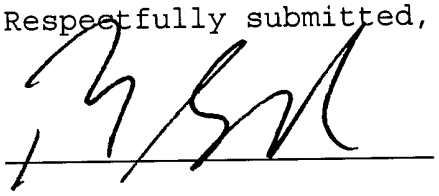
DNA duplexes". The reference does not contemplate the use of pH as a technique to create a stable reaction vessel. Therefore, it would not be obvious to someone skilled in the art to combine these two references, and the claims are not rendered obvious.

The examiner further objected to claims 1-5, 7, and 9 as being obvious in view of Anderson and Woodard references. Anderson was described earlier. Woodard discloses a glass fiber membrane that can bind DNA, and then allow elution of DNA from the membrane. Anderson does not describe a means for binding DNA. Rather, glass beads are provided as a physical decomposition agent that does <u>not</u> participate in the binding of DNA. If Woodard is combined with Anderson, a person skilled in the art could safely assume that the glass membrane is used in the same manner as the glass beads- not as a substrate means for binding the nucleic acid, but as a physical agent for grinding the starting material. In the instant claims, the glass membrane or substrate binds to the nucleic acid, and is partially responsible for the resolution and quality of the nucleic acid obtained in the invention. Thus, a combination of the two references would lead to an illogical and unpredictable result. The claims are not rendered obvious.

The examiner rejects claims 1-5, 7, 9, and 26 as being obvious in view of Anderson and Asgari references. Anderson was described above. Asgari describes a method of identifying a fetal red blood cell based on the presence of RNA in fetal hemoglobin. Asgari does not provide enough guidance as to the use of ammonium chloride in a lysis/buffer system. While Anderson discloses a buffer solution, Asgari does not describe the ammonium chloride in the context of a buffer system, but rather as a lysing agent. There is no evidence to support the reasonable combination of the references, since the examples in Asgari do not even mention the use of ammonium chloride. There is not enough guidance in Asgari to support the combination. Moreover, neither of the references cites ammonium chloride as an antichaotropic agent. Thus, the claims are not rendered obvious in view of the references.

Wherefore, allowance of the claims is earnestly solicited.

Respectfully submitted,



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